REMARKS

Entry of the foregoing amendments and favorable reconsideration of the subject application, pursuant to and consistent with 37 C.F.R. Section 1.112, and in light of the remarks which follow, are respectfully requested. This amendment is in response to the non-final Office Action mailed on September 11, 2008. Claims 1 and 6 have been amended, claims 2 and 3 have been canceled, and claims 4, 5 and 7 are pending. No new matter has been added by way of this amendment.

Foremost, the Examiner has rejected claims 1-7 under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner contends that "[n]one of the water insoluble alkyl cellulose ether derivatives[,] water insoluble acrylic polymer derivatives and water insoluble vinyl derivatives[,] other than those examples provided on page 4 [of the specification,] meet the written description due to lacking chemical structural information for what they are..." Office Action, pages 2-3. Moreover, the Examiner contends that the "specification provides insufficient written description to support the genus of derivatives encompassed by the claim..." *Id.* Applicants respectfully disagree.

Applicants submit that claims 1-7, as amended, clearly define the scope of the invention commensurate with the specification and that one skilled in the art would recognize that Applicants have invented the claimed subject matter. Indeed, the specification is clear that the "relatively water-insoluble macromolecular substance" can be any "water-insoluble macromolecular substance having [a] skin layer-forming property and ability to control the release of the drug." Application, page 4, lines 14-24. To this end, Applicants enumerate several categories of suitable water-insoluble macromolecular substances, and even provide specific

non-limiting examples within each category. *Id.* From this disclosure, one skilled in the art would recognize that other alkyl, vinyl, and acrylic derivatives would also be suitable and within the purview of this disclosure. Accordingly, this rejection should be withdrawn.

The Examiner has also rejected claims 1-7 under 35 U.S.C. 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Office Action, pages 3-4. Applicants respectfully disagree.

Applicants submit that claims 1-7 clearly define the scope of the invention such that the term "relatively water-insoluble macromolecular substances" as recited in the claims does not render the claims indefinite. In particular, the specification explicitly defines the term "relatively water-insoluble macromolecular substance" as follows:

> "In the present invention, the relatively water-insoluble macromolecular constituting the skin layer is a water-insoluble macromolecular substance having skin layer-forming property and ability to control the release of the drug."

Application, page 4, lines 14-17. This term, when read in of the context the specification, would reasonably apprise of ordinary skill in the art of the scope of the invention. Accordingly, the rejection should be withdrawn.

Claims 1-7 have also been rejected under 35 U.S.C. 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Office Action, page 4.

The Examiner believes that the term "one or more hot-melt low-melting substances" is contradictory with itself. This term, however, is defined in the specification. "The hot-melt low-melting substance constituting the skin layer is a hot melt substance having a relatively low melting point,

preferably a melting point of not higher than 70°C, more preferably from room temperature to 70°C, and ability to control the release of the drug." Application, page 4, line 25 to page 5, line 10. Claims 1 and 6, as amended, include a temperature limitation, as described in the specification, therefore rendering this rejection moot.

Claim 6 has also been rejected under 35 U.S.C. 112, second paragraph for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Office Action, pages 4-5. To address this rejection, Applicants have amended claim 6 to clarify that the first and second layers are cured to form films (step d) and that a plurality of granules are encapsulated in the capsule (step e). Accordingly, this rejection should be withdrawn.

Claims 1-7 have been rejected under 35 U.S.C. 103(a) as being unpatentable over JP 02226416A, CAPLUS Abstract to *Hara et al.* (hereinafter "*Hara*") and further in view of U.S. Patent No. 5,068,112 to *Samejima et al.* (hereinafter "*Samejima*") and U.S. Patent No. 5,837,291 to *Maruyama et al.* (hereinafter "*Maruyama*"). Office Action, pages 5-7.

The Examiner contends that *Hara* teaches an oral preparation of beraprost sodium in which granules of lactose and corn starch are coated with EUGRAGIT® S-100 and dried. The Examiner states that *Hara* is missing three discrete elements of the claimed invention. Office Action, page 6. The Examiner, however, relies on the secondary references to cure these deficiencies. Specifically, the Examiner believes that it would have been obvious to one of ordinary skill in the art to combine the "enteric" beraprost sodium granules of *Hara* with the waxes of *Maruyama*, and the granule sizes of *Samejima* to arrive at the present invention. Applicants respectfully disagree.

Foremost, while beraprost sodium, waxes, granule sizes, and methods for controlled release of a drug are undoubtedly known individually in the pharmaceutical industry industry, the art of record certainly does not suggest combining such elements to arrive at the instant invention in the way that the Examiner contends would have been obvious. As such, the Patent Office's contention that one of skill in the art would be motivated to combine the missing elements of the secondary references with *Hara* is unsupported.

In fact, all that the Patent Office has done was to find the individual elements of the claimed invention in discrete prior art references and, using only Applicants' claims and disclosure as a guide, argued that the teachings, if combined, would produce the claimed invention. Indeed, the Patent Office would appreciate that many of the of the elements required by the claimed invention, that is, 1) the size of the granules, 2) the encapsulation of the granules into a capsule and 3) the presence of a second coating layer containing one or more hot-melt low-melting substances, are missing from *Hara*, as admitted by the patent Office. Office Action, page 6. As such, about half of the elements required by the claimed invention are missing. Such a hindsight construction is not permitted and does not constitute a *prima facie* case of obviousness. Moreover, there is no reason, apart from a retrospective view of the art using Applicants' application as a road map, to select these elements.

In fact, even if combined, the references do not suggest a pharmaceutical composition comprising a plurality of granules having diameters of not more than 1000 μm, wherein the granules comprise a nucleus granule comprised of beraprost sodium, a coating agent coating the nucleus granule, wherein the coating agent is comprised of a first skin layer containing one or more relatively water-insoluble macromolecular substances selected from the group consisting

of water-insoluble alkyl cellulose ether derivatives, water-insoluble acrylic polymer derivatives and water-insoluble vinyl derivatives, and a second skin layer containing one or more hot-melt low-melting substances, the hot-melt low-melting substances having a softening point of not higher than 70°C, or a process for producing such a composition. Specifically, the teaching of *Maruyama*, that hydrophobic waxes "can be *added to the enteric coating* to improve the water resistant of the obtained enteric preparation" does not in any way suggest a first skin layer and a second skin layer as disclosed and claimed in the present invention. *Maruyama*, column 2, line 66 to column 3, line 3 [emphasis added]. The Patent Office provides no basis for one to even speculate that such a combination would provide desirable results or that such a combination would even be capable functioning as composition similar to the claimed invention.

Additionally, claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Hara* and further in view of *Samejima* and U.S. Patent No. 5,405,617 to *Gowan Jr. et al.* (hereinafter "*Gowan*"). The Examiner further contends that it would have been obvious to combine the "enteric" beraprost sodium granules of *Hara* with the granule sizes of *Samejima* and the taste mask coating or carrier comprising an aliphatic or fatty acid ester of *Gowan* to arrive at the present invention. Office Action, page 9. Applicants respectfully disagree.

This rejection is based on an improper attempt at hindsight reconstruction. Specifically, *Gowan* teaches a solventless taste masking carrier or coating composition which is completely unrelated controlled release composition of the present invention. The solventless taste masking coating or carrier of *Gowan* has nothing whatsoever to do with solving the problems involved with Applicants' discovery of sustained

release, high bioavailability, pH insensitive, beraprost sodium compositions and methods of making such compositions. Accordingly, the Examiner should withdraw this rejection.

Moreover, even if the references were combined, there is no reasonable expectation that such a combination would yield the claimed invention. The Patent Office fails to provide any basis for their assumption that the combination of an enteric coated core and a taste masking compound would result in a composition or method that would achieve the results of the claimed invention. The Office provides no basis for one to even speculate that such a combination would provide desirable results or that such a combination would even be capable functioning as composition similar to the claimed invention.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

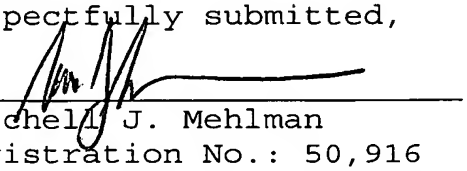
As it is believed that all of the rejections set forth in the Office Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he/she telephone Applicants' attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: December 11, 2008

Respectfully submitted,

By 

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